REMARKS

Claims 1, 2, 4-7, 34, and 36 have been amended. Support for the amendments to the claims can be found throughout the specification as filed, e.g. in original claim 35, p. 6, lines 26-27, and p. 7, lines 4-6. Claims 3 and 8 as well as claims 12-33 and 38-51 have been canceled without prejudice. Applicants reserve the right to pursue the canceled subject matter in one or more continuing applications. Upon entry of the proposed amendment, claims 1, 2, 4-7, 9-11, and 35-37 will be pending.

Objection to the Specification

The specification was objected to for lacking a SEQ ID NO: where the amylin peptide sequence is presented. Applicants note that a SEQ ID NO: was added at page 1, line 25, by the amendment to the specification filed with the Response to Notice to Comply with Requirements on January 15, 2002. Applicants ask that this objection be withdrawn.

Rejections Under 35 U.S.C. § 101

Claim 41 was rejected for lacking claimed recitation of a use. This claim has been canceled, thereby obviating the rejection.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-11, 34-37, and 41 were rejected for indefiniteness. Claims 1-3 were rejected for containing the phrase "the active concentration" without antecedent basis and without defining effective concentration. This phrase has been amended to "amylin activity"and the claims specify that amylin activity is increased in an amount sufficient to stimulate chondrocyte proliferation.

Claim 6 and dependent claims were rejected for containing the generic term, "analog". The claims have been amended to include the limitation wherein the amylin analog is "a fragment of amylin comprising amylin (1-8) (SEQ ID NO:2)". As this limitation is clear, the claims are defined.

Claim 34 was rejected for lack of clarity regarding whether the claimed method or recited amount of amylin administered is effective. The amendment to this claim specifies that the claimed amount is effective.

Claim 41 was rejected for lacking steps. This claim has been canceled.

The amendments to the claims address each of the rejections. Withdrawal of these rejections is requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 6-10, 34-36, and 41 were rejected for lack of written description. The Examiner stated:

> The claims are broadly drawn to a method of facilitating bone or cartilage growth comprising administering to a subject amylin analog or amylin mutant or derivative (e.g., insertion of a heterologous polypeptide that is structurally irrelevant to amylin *per se*). There is insufficient guidance and direction as to make and use amylin analogs...The specification is silent in characterization of amylin analogs (variants) having comparable activity of unmodified amylin molecules.

This rejection is traversed. Applicants have narrowed the claims to methods of treating patients with amylin or amylin analogs, the amylin analogs being fragments of amylin comprising amylin (1-8). Thus, the claims are directed to methods comprising administering analogs that include a specific region of the peptide. Fragments of amylin that include amylin (1-8) are characterized in the specification, and have been shown to have activity comparable to that of the full-length amylin peptide. See, for example, the passage at page 13, lines 8-24, of the specification, which describes experiments in which amylin (1-8) was shown to increase tibial growth in vivo to levels comparable to those induced by amylin (i.e., amylin (1-8) stimulated an increase in the width of tibial growth plates from 0.081 mm to 0.111 mm, and amylin stimulated an increase from 0.083 mm to 0.108 mm).

The Examiner asserted that the claims are not supported by description of a "core structure" and that they lack meaningful, distinguishing characteristics. Applicants disagree. The specification is not silent in characterization of the analogs for use in the claimed methods.

The specification discloses the structure (i.e., the amino acid sequence) of fragments of amylin comprising amylin (1-8). The functional properties of these peptides (e.g., stimulation of chondrocyte proliferation), methods of making the peptides, and correlation between structure and function is provided by the specification and the claims. The limitation requiring that the analogs include amylin (1-8) describes a "core structure".

According to the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pp. 1106, Friday, January 5, 2001), the Examiner should determine whether the application describes a reduction to practice, whether it describes the structure of the invention as a whole, and whether there is a description of a

> representative number of species by reduction to practice, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics...

Applicants have satisfied these requirements. For example, multiple species of the amylin compositions for use in the methods have been reduced to practice, identifying characteristics and structural properties of the genus of compositions have been provided (i.e., the structural requirement for amylin (1-8)), and functional properties are noted. Thus, the claims are described. Applicants ask that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 102

Claims 1-7, 8-10, 34-36, and 41 were rejected as anticipated by Reid et al., WO 96/02269 ("Reid") [1]. The Examiner stated:

> Reid et al. teach a method of treating a patient in need of stimulating bone growth comprising administering amylin or amylin agonist to the patient...Note that the above-mentioned claims are anticipated by the Reid et al. teachings because the Reid et al. method for stimulating bone growth comprises the same step, i.e.,

[1] Claims 34-36 are directed to methods of stimulating chondrocytes in vitro including administering amylin or an amylin analog which is a fragment of amylin comprising amylin (1-8). Reid does not disclose any methods in which chondrocytes are cultured in vitro, much less methods in which chondrocytes are stimulated in vitro by amylin activity. Applicants believe the rejection of claims 34-36 is improper.

administering amylin to the patient wherein administration of amylin to the patient inevitably lead to augmenting chondrocyte proliferation since the consequence of the administration, i.e., stimulating bone growth and chondrocyte proliferation (a part of bone growth) is inherent in the step of the method; the same method comprising the same composition and steps must result in the identical endpoint.

This rejection is respectfully traversed. Claims 1-7, and 9-10 are directed to methods of treating patients to stimulate chondrocyte and/or stimulate cartilage growth or repair[2]. The methods include increasing amylin activity, e.g., by administering amylin or an amylin analog which is a fragment of amylin comprising amylin (1-8). Applicants have recognized that increasing amylin activity stimulates chondrocyte proliferation and can be useful, e.g., in the treatment of patients suffering from cartilage defects. Accordingly, Applicants claim methods wherein a patient is treated by increasing amylin activity.

The Examiner stated that the claimed methods are inherent in Reid because administration of amylin inevitably has the effect of stimulating chondrocyte proliferation, as part of bone growth. Applicants disagree that stimulating chondrocyte proliferation as part of bone growth inherently anticipates the claims. Inherency requires that a person of skill would automatically recognize that missing descriptive matter is necessarily present in a reference. Reid does not disclose any methods "to stimulate chondrocyte proliferation" (a limitation of all rejected claims) or "to stimulate cartilage growth or repair" (a limitation of claims 2 and 7) and Reid is unaware that increasing amylin activity would have these effects. Reid shows that amylin stimulates bone growth by stimulation of osteoblast proliferation. Reid does not recognize that amylin has an effect on chondrocytes. Nor does Reid recognize that amylin would be useful for stimulating cartilage growth. There is nothing in Reid that would lead one of skill to perform a method to stimulate chondrocyte proliferation and/or cartilage growth or repair.

One would not have necessarily recognized that amylin would have an effect on chondrocyte proliferation from the disclosure of Reid, because Reid only shows that amylin affects osteoblasts, and Reid fails to indicate that amylin can be used in methods of stimulating

[2] Claims 3 and 8 have been canceled.

chondrocytes or cartilage. Chondrocytes are a different cell type than osteoblasts, and they mediate a distinct set of biological activities in the body. There is no indication that osteoblasts and chondrocytes would respond to a given biological mediator in an identical fashion, and that the physiological results would be the same. Reid is completely silent as to any effect of increasing amylin activity on chondrocytes and cartilage. Therefore, Reid et al. does not anticipate the claims.

Obviousness-type Double Patenting

Claim 8 and 9 were rejected for provisional obviousness-type double patenting over U.S. Pat. No. 5,922,677. This rejection is traversed. Claim 8 has been canceled, therefore the rejection is moot as it applies to claim 8. Claim 9 depends from claim 6, which is directed to a method for treating a patient to stimulate chondrocyte proliferation in vivo. Claims of U.S. Pat. No. 5,922,677 are directed to methods of stimulating bone growth by administering amylin. Claim 9 is not an obvious variation of claims of U.S. Pat. No. 5,922,677 because, for reasons discussed above, it is not obvious that stimulation of bone growth necessarily includes stimulation of chondrocyte proliferation. The biological effects of stimulating chondrocytes and osteoblasts differ, as do the distribution of these cell types in the body. Chondrocytes mediate cartilage growth, among other things. None of the claims of U.S. Pat. No. 5,922,677 mention chondrocytes. Indeed, neither the claims nor the specification of U.S. Pat. No. 5,922,677 disclose a method of stimulating chondrocyte proliferation by administering amylin. Withdrawal of this rejection is therefore requested.

Enclosed is a $950 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 6-3-04

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